II. RESPONSE TO OFFICE ACTION

A. State of the Claims

Claims 53-58, 60-62, 68-80, 97-102, 109, 112-114, 123, and 137-143 were pending prior to the instant Office Action. However, claims 53-58, 60-62, and 68-80 have been withdrawn from consideration as being drawn to a non-elected invention. Therefore, claims 97-102, 109, 112-114, 123, and 137-143 were the subject of the instant Office Action.

Claims 97, 109, 123, and 137 have been amended in the amendment disclosed herein. New claims 144-156 have been added. Support for the amended claims and new claims can be found throughout the Specification. Therefore, claims 97-102, 109, 112-114, 123, 137-156 are presently pending.

B. Formal Matters

The Action notes that a Final Office Action as mailed on August 19, 2002. However, upon further consideration by the Examiner, the finality of that Action was withdrawn and prosecution on the merits has been allowed to continue.

C. The Rejections Under 35 U.S.C. §112, First Paragraph, are Overcome

1. The Written Description Rejections are Overcome

a. Background and Rationale for the Rejections

The Action maintains a rejection of claims 97-102 for the reasons of record noted in the Final Office Action. Due to the fact that approximately 300 known residues of the protein encoded by SEQ ID NO:11 are 95% identical to the homologous portion of the fully characterized mouse kappa opioid receptor encoded by SEQ ID NO:1, and the fact that the

second extracellular loop of each of these receptors is 100% identical, the rejection of claims 109, 112-114, 123, and 137-143 under 35 U.S.C. §112, first paragraph, has been withdrawn.

According to the Action, Applicants' argument that the processes of claims 97-102 pertain to fragments of SEQ ID NO:11, and that the entire full-length sequence of an opioid receptor is not required to practice the claimed invention were not found persuasive. The Action indicates that, without being in possession of the entire full-length opioid receptor sequence, it is not known how Applicants can accurately determine that a compound is an agonist, or an antagonist of the receptor, as the present invention claims. As a result, the recitation of an entire full-length sequence of an opioid receptor is said to be required.

The claims at issue pertain to processes for screening a substance for its ability to specifically bind to an opioid receptor utilizing recombinant opioid receptor polypeptides encoded by at least 30 contiguous bases from a specific polynucleotide sequence, SEQ ID NO:11. The nucleic acid sequence of SEQ ID NO:11, which is a partial genomic sequence of a human opioid receptor, is fully disclosed in the Specification.

At issue is the Examiner's assertion that Applicants must have disclosed the <u>entire sequence of a full-length opioid receptor</u> at the time of filing in order to meet the written description requirement. In the present Office Action, the Examiner indicates that Applicants must describe the entire full-length sequence of an opioid receptor since the claims are "reach through" claims, as Applicants are attempting to receive patent protection on the full-length opioid receptor even though they are not in possession of this receptor. Office Action, page 4, paragraph 1. The Examiner has also previously argued that in order for the claims to encompass various constructs such as chimeras, Applicants would either need to use "consisting of"

language or recite that the nucleic acids of the claimed processes would only be able to "comprise" up to the full length of SEQ ID NO:11.

Applicants traverse this rejection for the reasons set forth below.

b. Examiner's Burden and the Law Pertaining to Written Description

It is well-established that the inquiry of whether the written description requirement of 35 U.S.C. §112, first paragraph, must be determined on a case-by-case basis and is a question of fact. *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). The Federal Circuit has stated that the test for the written description requirement is "whether the application relied upon 'reasonably conveys to the artisan that the inventor had possession at the time of the later claimed subject matter.'" *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790 (Fed. Cir. 1998). See also *Markman v. Westview Instruments, Inc.* 52 F.3d 967, 34 USPQ 2d 1321 (Fed. Cir. 1995) (en banc) ("Claims must be read in view of the Specification, of which they are a part.").

In rejecting a claim under the written description requirement of 35 U.S.C. §112, first paragraph, the Examiner has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined in the claims. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). In rejecting a claim under written description, the Examiner is required: (1) to set forth the claim limitation not described; and (2) to provide reasons why a person skilled in the art would not have recognized the description of the limitation in view of the disclosure of the application as filed. *Interim Guidelines for the Examination of Patent Applications Under 35 USC 112, Paragraph 1*, Chisum on Patents, vol. 3, §7.04[1][c].

c. The Examiner has Failed to Meet his Initial Burden

The Examiner has failed to meet his initial burden of presenting evidence of why a person skilled in the art would not recognize in Applicants' disclosure a description of the invention defined in the claims. The Examiner has indicated that the claim limitation not described is the entire sequence of a full-length opioid receptor, which is not recited in the claim. Applicants' Specification fully meets the written description requirement of 35 U.S.C. 112, first paragraph, for the reasons set forth below.

d. The Specification Discloses Full-Length Opioid Receptors

Applicants' Specification provides written description support for full-length human opioid receptors. For example, the background section of the Specification provides substantial information pertaining to the structure and function of opioid receptors. Specification, page 3, line 20 through page 11, line 8. The major classes of opioid receptors are discussed, including properties of these different classes. Specification, page 3, line 20 through page 5, line 15. Binding properties and structural characteristics of opioid receptors are also discussed. Specification, page 5, line 17 through page page 11, line 8.

In addition, the Specification discloses a recombinant opioid receptor encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. Those of ordinary skill in the art understand that an opioid receptor must have certain functional characteristics. In addition, those of ordinary skill in the art would be familiar with the function of opioid receptors, which is described throughout the Specification, as noted above. Thus, functional full-length opioid receptors are fully supported by the Specification.

e. Disclosure of an Entire Full-Length Sequence of Such a Receptor is Not a Requirement for Adequate Written Description of the Present Claims

Even though Applicants' Specification discloses full-length opioid receptors, the disclosure of the entire sequence of a full-length opioid receptor in the Specification is not required for one of skill in the art to recognize the invention. The present invention is drawn to methods of screening a substance for its ability to specifically bind to an opioid receptor by contacting the substance with an opioid receptor polypeptide encoded by a nucleic acid sequence that has all or part of the contiguous bases of SEQ ID NO:11. Thus, the Specification satisfies the written description requirement because it reasonably conveys to one of skill in the art that Applicants had possession of the claimed subject matter. *In re Daniels*, 144 F.3d 1452, 1456, 46 USPQ2d 1788, 1790.

The preamble of claim 97 recites that the claim involves "a process of screening a substance for its ability to specifically bind to an opioid receptor." The process comprises the steps of: (1) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; (2) contacting the substance with the opioid receptor polypeptide; and (3) detecting whether said substance has an ability to specifically bind to said opioid receptor polypeptide.

The process pertains to polynucleotides that are encoded by at least 30 contiguous bases of SEQ ID NO:11. The Specification ***fully discloses*** SEQ ID NO:11. By formulating a rejection for failure to recite the entire sequence of a full-length opioid receptor and making reference to "reach through claims," the Examiner appears to suggest that knowledge of the entire sequence of a full-length opioid receptor is required to practice the claimed invention. However, this is ***not*** the case.

As per claim 97, a substance is contacted with an opioid receptor polypeptide that is encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11, and the ability of the substance to bind to this opioid receptor polypeptide is detected. The opioid receptor polypeptide that is encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11 need not be a full-length opioid receptor polypeptide. If a substance is contacted with this polypeptide, and binding is detected, then the substance can be said to bind to an opioid receptor polypeptide. If a substance binds to such opioid receptor polypeptide, then it would bind to a full-length opioid receptor polypeptide. Disclosure of the entire sequence of a full-length opioid receptor is not required. In order for the Specification to fully support the claimed process, the Specification must fully disclose SEQ ID NO:11, which it does. Thus, the Specification fully supports the claimed process, which pertains to SEQ ID NO:11.

f. Written Description for Determining Whether a Compound is an Agonist or Antagonist is Not Required

The Examiner has also indicated in the present Office Action that without being in possession of the entire sequence of a full-length opioid receptor, it is not known how Applicants can accurately determine that a compound is an agonist, or an antagonist of the receptor, as the present invention claims. Applicants find this rationale to be illogical.

Independent claim 97 pertains to "[a] process of screening a substance for its ability to specifically bind to an opioid receptor ..." Limitation (c) of claim 97 involves "detecting whether said substance has an ability to specifically bind to said opioid receptor polypeptide." The remaining claims at issue in this rejection depend from claim 97. No where in the claim is there a recitation of a requirement that it must be determined whether the substance is an agonist

or an antagonist of the receptor. Rather, the claims only pertain to binding of the substance to the recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. The Examiner appears to be arguing for inadequate written description support for a limitation that is not present in the claims at issue. Thus, a rejection for inadequate written description based on inability to determine whether a compound is an agonist or an antagonist is misguided.

g. "Consisting of" Language is Not Required

The Examiner indicates that in order for their claims to encompass genetic constructs that encompass the entire length of a human opioid receptor, that Applicants would either need to use "consisting of" language or recite that the nucleic acids of the claimed processes would only be able to "comprise" up to the full length of SEQ ID NO:11. Thus, the Examiner seems to be requiring that use of the term "comprising" as the transitional phrase requires that all possible embodiments of the invention that the claim reads upon must be disclosed in the Specification. By the Examiner's reasoning, for example, any claim to a polypeptide comprising a particular newly discovered amino acid sequence wherein the amino acid sequence is fully disclosed in the Specification could <u>never</u> be claimed since it is possible that the amino acid sequence might at some later point in time be attached to an object that is not presently disclosed in the Specification. Let us assume, for example, that this unknown object is a spaceship. Since the Specification not only fails to disclose a spaceship, but fails to disclose how to construct a spaceship, then by the Examiner's logic there is no written description support in the Specification for the polypeptide. This faulty logic used by the Examiner fails to take into

account the Applicants' claim limitations. The claim limitations recite SEQ ID NO:11 in the claimed process, and not a full-length opioid receptor.

h. The Present Claims and Specification are in Accordance with *University of California v. Eli Lilly and Co.*

In making the written description rejection, the Examiner also indicates that because the claim language includes "opioid receptor," that by necessity a full-length opioid receptor must be described in the Specification. Such an interpretation of the written description is faulty and erroneous. In particular, the Examiner appears to be misapplying the requirements of written description set forth in *University of California vs. Eli Lilly and Co.*, which requires that claims to genetic material require recitation of more than a mere function. *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) ("In claims to genetic material, however, a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function.")

While it is true that in claims to genetic material, a generic statement without more is not an adequate written description of the genus, the claims recite more than a mere function. In particular, the full nucleic acid sequence of SEQ ID NO:11 is disclosed in the Specification. In addition, there is full support for all claim limitations in the Specification. Thus, Applicants are fully in compliance with the written description requirements set forth in *Eli Lilly* because the claimed process of screening utilizing polypeptides encoded by at least 30 contiguous bases of SEQ ID NO:11 is fully supported by the Specification, particularly since SEQ ID NO:11 is disclosed in the application as are the claimed process, and furthermore, one of skill in the art

would be able to practice the claimed invention based on the existing disclosure without additional disclosure of the entire sequence of a full-length opioid receptor.

i. Applicants Do Not Need to Describe Every Embodiment Upon which the Claims Read

The Examiner requires disclosure of the entire sequence of a full-length opioid receptor. As discussed above, Applicants have disclosed full-length opioid receptors in their Specification.

In requiring the disclosure of the entire sequence of a full-length opioid receptor, the Examiner seems to be requiring that every embodiment or a specific embodiment covered by a claimed invention be disclosed. Applicants know of no such requirement, and invite the Examiner to provide case law in support of this proposition. Nor does patent law require Applicants to limit their invention to embodiments reduced to practice, as suggested by the Examiner.

Applicants do not need to describe in their Specification every size embodiment on which the claim reads. In fact, according to the Federal Circuit, "[i]t is well-established that a patent applicant is entitled to claim his invention generically, when he describes it sufficiently to meet the requirements of section 112." *Amgen v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2D 1016, 1027 (Fed. Cir. 1991) ; *See also Utter v. Hiraga*, 856 F.2d 993, 998, 6 USPQ2D 1709, 1714 (Fed. Cir. 1988) ("A Specification may, within the meaning of 35 U.S.C. §112, paragraph 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses.")

The written description requirement has been extensively addressed by the Federal Circuit. In particular, the Federal Circuit has stated that "[t]he written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the

description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.'" *Union Oil Co. of California v. Atlantic Richfield Co.*, 208 F.3d 989, 997, 54 USPQ 2d 1227, 1232 (Fed. Cir. 2000). The Federal Circuit has also noted that "[if] a person or ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the Specification, then the adequate written description requirement is met." *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996).

Applicants are in accordance with the Federal Circuit's requirements pertaining to written description, as one of ordinary skill in the art would have understood that Applicants were in possession of a screening process involving "30 contiguous bases of SEQ ID No.: 11." In fact, the Examiner admits this much.

Regardless of what other protein components are added to those specifically provided, the full scope of the method as claimed was in possession of the inventors because the full scope of the invention is determined by the unique functional and structural characteristics of the compositions recited. That is, one may screen for or isolate substances that specifically bind to an opioid receptor, act as receptor agonists and the like, using the polynucleotides and polypeptides as claimed (as is fully described by the Specification).

In the present case, it is irrelevant whether additional sequences are attached to the compositions claimed as part of the methods because such additional sequences have not been claimed *per se*. If such a rejection were proper, "comprising" claim language could not be used with any claim, because in the case of nearly any composition or method it is possible to attach thereto some additional component of potentially unlimited size, which is itself not described in the application. What is relevant is that the claimed subject matter has been adequately

described in a manner that reasonably conveys to one skilled in the art how to make and use the invention.

j. Applicants Have Demonstrated Possession of SEQ ID NO:11

Applicants submit that the proper issue is not whether Applicants had in their possession the entire full length receptor sequence that comprises SEQ ID NO: 11, but rather whether they had possession of the invention including compositions comprising SEQ ID NO: 11, sub-sequences thereof, and methods of using such compositions to screen for substances that bind them. The Action agrees that Applicants had possession of SEQ ID NO: 11. Applicants have already cited sections of their Specification which demonstrate that they were in possession of the disclosed sequences as well as other aspects of the claimed processes. "It is possible to create an almost endless array of chimeras using standard genetic manipulations and the knowledge that the inventors have derived concerning the ligand binding sites of the opioid receptors. All such chimeras, the polynucleotides encoding them, and methods of using them in assays are contemplated within the scope of the invention." Page 170 of the Specification, lines 9-14.

The Examiner has indicated that Applicants intend to hunt for the remaining portion of the DNA while inhibiting those who may actually have identified the full-length receptor from claiming it. Applicants point out that they are claiming screening methods that utilize the novel and non-obvious characteristics of the nucleotides and polypeptides disclosed and the rejections must be relevant to the claimed invention. The present claims would not inhibit those who practice methods utilizing solely the balance of the receptor (or other polypeptide) exclusive of that claimed.

Applicants submit that the full scope of the present invention is described in the Specification as filed. There is no "substantial evidence" to support the Examiner's position on Appeal, and as a result the Examiner's position should not be upheld. *In re Gartside*, 203 F.3d 1305, 1315 (Fed. Cir. 2000).

k. Conclusion

In view of the above remarks and arguments, it is requested that the written description rejections be withdrawn.

2. The Enablement Rejections are Overcome

a. Background and Rationale for the Rejections

Claims 97-102 are newly rejected under 35 U.S.C. §112, first paragraph, because the Specification, while being enabling for a process of screening antibodies, is said to not reasonably provide enablement for a process of screening for agonists, antagonists, or any other compound which are known to require specific regions of the human kappa opioid receptor for binding or activity. According to the Action, the Specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

b. Examiner's Burden and the Law Pertaining to Enablement

The test of enablement is whether the disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976); *MPEP* §2164.01.

c. The Specification Contains Substantial Information Regarding the Subject Matter of the Claims

The Specification contains sufficient information regarding the subject matter of the claims to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. Substantial information pertaining to processes for screening a substance for its ability to specifically bind an opioid receptor can be found throughout the Specification. The entire polynucleotide sequence of SEQ ID NO:11 is found in the Specification. Examples 1-8 provides substantial information pertaining to opioid receptors and opioid receptor polypeptides, opioid receptor isolation, and opioid receptor binding studies. Specification, page 121, line 17 through page 154, line 28. Example 10 provides information pertaining to the binding domains of the Kappa receptor, and assays for binding to the receptor. Specification, page 165, line 26 through page 171, line 26.

d. Applicants are Not Required to Disclose a Full-Length Human Opioid Receptor in Order to Enable the Claimed Invention, But They Do

The Action indicates that without guidance or working examples as to what residues are required to practice the invention of claim 97, it is not predictable to the artisan as to what residues would be required to practice the invention of claim 97. However, the Specification fully meets the enablement requirement of 35 U.S.C. §112, first paragraph.

Even though Applicants are not required to disclose a full-length human opioid receptor to enable the claimed invention, they do so. As discussed above, the Specification contains substantial information pertaining to opioid receptors, including their functional characteristics.

Nevertheless, Applicants are not required to disclose a full-length opioid receptor in order to enable their claims.

The preamble of claim 97 recites that the claim involves "a process of screening a substance for its ability to specifically bind to an opioid receptor." The process comprises the steps of: (1) expressing a recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11; (2) contacting the substance with the opioid receptor polypeptide; and (3) detecting whether said substance has an ability to specifically bind to said opioid receptor polypeptide.

The process, rather than requiring use of a full-length human opioid receptor polynucleotide sequence, pertains to polynucleotides that are encoded by at least 30 contiguous bases of SEQ ID NO:11. The Specification ***fully discloses*** SEQ ID NO:11. The Examiner believes that knowledge of a full-length opioid receptor sequence is required to practice the claimed invention. However, this is ***not*** the case. The Specification fully enables Applicants' claimed process, which pertains to SEQ ID NO:11 and not the entire sequence of a full-length opioid receptor. Disclosure of the entire sequence of a full-length opioid receptor in the Specification is not required for one of skill in the art to recognize the invention.

The present invention is drawn to methods of screening a substance for its ability to specifically bind to an opioid receptor by contacting the substance with an opioid receptor polypeptide encoded by a nucleic acid sequence that has all or part of the contiguous bases of SEQ ID NO:11. As noted above, Applicants are not required to specifically disclose the entire sequence of a full-length human opioid receptor to enable the claimed invention. The full-length opioid receptor disclosed in claim 97 is one which is a recombinant opioid receptor encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11, as disclosed in

the Specification. One of ordinary skill in the art would understand that an opioid receptor must have certain functional characteristics. One of ordinary skill in the art would be familiar with the function of opioid receptors, which is described throughout the Specification. For example, functional characteristics of opioid receptors are described in the Background section of the Specification on pages 2 through 10. Thus, the claims at issue are enabled by the Specification and the knowledge of one of ordinary skill in the art.

Thus, Applicants' Specification satisfies the enablement requirement because it provides sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention without undue experimentation. *In re Angstadt*, 537 F.2d 498, 504, 190 U.S.P.Q. 214, 219 (CCPA 1976); *MPEP* §2164.01.

The claims, as currently written, are fully enabled by the Specification. As set forth above, in view of the disclosure in the Specification and the level of skill of an ordinary artisan, no undue experimentation is required. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). No undue experimentation would be required for one of ordinary skill in the art to practice the claimed invention, in view of the disclosure in the Specification.

e. The Rejection Based on Inability to Determine Whether a Compound is an Agonist or an Antagonist is Improper

The Examiner has also indicated that the Specification does not reasonably provide enablement for a process of screening for agonists, antagonists, or compounds other than antibodies which are known to require specific regions of the human kappa opioid receptor for binding or activity. Independent claim 97 pertains to "[a] process of screening a substance for its ability to specifically bind to an opioid receptor ..." Limitation (c) of claim 97 involves

"detecting whether said substance has an ability to specifically bind to said opioid receptor." The remaining claims at issue in this rejection depend from claim 97. No where in the claim is there a recitation of a requirement that it must be determined whether the substance is an agonist or an antagonist of the receptor. Rather, the claims only pertain to binding of the substance to the recombinant opioid receptor polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. The Examiner appears to be arguing for inadequate enablement for a limitation that is not present in the claims at issue. Thus, a rejection for inadequate enablement based on inability to determine whether a compound is an agonist or an antagonist is misguided.

f. Conclusion

In view of the above, the Specification provides sufficient enablement for the claimed invention. Accordingly, Applicants request that the enablement rejections under 35 U.S.C. §112, first paragraph, be withdrawn.

3. The New Claims are Allowable

The Action indicates that "[w]ithout further describing in the claims the regions required for the binding of compounds other than ligands, or without limiting the claims to recite a method of screening for antibodies only, this rejection is maintained." Office Action, page 3, paragraph 1. In addition, according to the Action, Applicants have provided adequate written description of regions such as the second extracellular loop. Office Action, page 3, paragraph 1.

In addition, the instant Action notes that the Specification is enabling for a process of screening antibodies. Office Action, page 4, paragraph 2. The Action also indicates that there is

enablement for methods involving proteins that comprises the second extracellular loop of SEQ ID NO:12. Office Action, page 4, paragraph 4.

New independent claim 144, which pertains to a process of screening a substance for its ability to specifically bind to an opioid receptor that involves expressing a recombinant opioid receptor polypeptide comprising the second extracellular loop comprising the amino acid sequence of residues 111 through 136 of SEQ ID NO:12 and encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11, has been added. New claims 145-149, which depend from claim 144, have also been added. In addition, new dependent claim 150, which pertains to a process of screening an antibody for its ability to specifically bind to an opioid receptor, has been added.

The Action appears to indicate that omission of reference to "opioid receptor" may make the claims allowable. New independent claim 151 has been added. New independent claim 151 omits "opioid receptor" from the claim language. In addition, new dependent claims 152-156, which depend from claim 151, have been added. As discussed above, there is adequate written description support throughout the Specification for these new claims. In addition, as discussed above, these claims are enabled. By adding these new claims, Applicants in no way concede that the other claims are not allowable.

Therefore, the new claims are allowable.

D. The Rejections Under 35 U.S.C. §112, Second Paragraph, are Overcome

Claims 109, 112-114, 123, and 137-143 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the Action, which cites *MPEP* §

2172.01, claims 109 and 112-114 are rejected as being incomplete for omitting essential steps that amounts to a gap between the steps. The Action states that the omitted step is a method step for isolating the claimed substance. In addition, claims 109, 112-114, 123, and 137-143 are rejected under 35 U.S.C. §112, second paragraph, as being incomplete for omitting the step of a method for determining that the isolated substance is an agonist. Applicants traverse these rejections.

According to *MPEP* § 2172.01, "[a] claim which fails to interrelate essential elements of the invention as defined by Applicants in the Specification may be rejected under 35 U.S.C. §112, second paragraph, for failure to point out and distinctly claim the invention." *MPEP* § 2172.01, citing *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976).

Claim 109, subpart c, now includes the limitation "detecting whether said substance has an ability to agonize said opioid receptor polypeptide." In addition, subpart d of claim 109 now recites "isolating said substance if said substance has an ability to agonize the opioid receptor polypeptide." Claim 137 now includes the limitation "detecting whether the substance has an ability to agonize the opioid receptor polypeptide." In view of these limitations, there is no incomplete or omitted step in claim 109 or 137, or in any of the claims that depend from these claims.

In claim 109, recitation of a specific method for isolating the substance is not required under *MPEP* § 2172.01. In claims 109 and 137, recitation of a precise method for determining that the substance is an agonist is not required under MPEP § 2172.01. Any method known to those of ordinary skill in the art for isolating the substance or for determining whether the substance is an agonist can be used in practicing the claimed invention. Furthermore, each of the

limitations recited in the claims is interrelated in a manner that is sufficient to practice the claimed invention.

Regarding agonist activity, it should be noted that binding to the opioid receptor polypeptide is indicative of functional agonist activity. The opioid receptor polypeptide of claim 109 (and similarly, the chimeric opioid receptor polypeptide of claim 137) comprises the second extracellular loop comprising amino acid sequence residues 111 through 136 of SEQ ID NO:12 and encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. The Specification notes that "[m]ore preferably, the opioid receptor polypeptide comprises a portion of a second extracellular loop of the kappa opioid receptor polypeptide, ***which has been shown to have a binding site for kappa receptor-specific agonists***." (emphasis added). Therefore, binding to a portion of the second extracellular loop of the kappa opioid receptor is highly indicative of functional agonist activity. As noted above, one of ordinary skill in the art would be able to detect, using any method known in the art, whether the substance has an ability to agonize the opioid receptor polypeptide.

Similarly, for the reasons set forth above, new claims 151-156 are not indefinite. No essential steps are omitted for practice of the claimed invention. Claim 151 includes the limitation "detecting whether the substance has an ability to specifically bind to said recombinant polypeptide encoded by a nucleic acid sequence comprising at least 30 contiguous bases of SEQ ID NO:11. Recitation of a precise method to detect binding is not required to practice the claimed invention. Any method known to those of ordinary skill in the art can be used to detect binding.

With regard to claim 123, Applicants have amended the claim to correct a typographical error. Specifically, the claim has been amended to depend from claim 113 rather than claim 143.

For all of these reasons, the rejections under 35 U.S.C. §112, second paragraph, should be withdrawn.

E. Conclusion

Applicants believe that the foregoing remarks fully respond to all outstanding matters for this application. Applicants request that the rejections of all claims be withdrawn so they may pass to issuance.

Should the Examiner desire to sustain any of the rejections discussed in relation to this Response, the courtesy of a telephonic conference between the Examiner, the Examiner's supervisor, and the undersigned attorney at 512-536-3081 is requested.

Respectfully submitted,

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